Claims

1. An isolated MAGE-A12 HLA class I-binding peptide comprising the amino acid sequence of SEQ ID NO:6, or a functional variant thereof which binds HLA class I molecules comprising one or more amino acid additions, substitutions or deletions.

2. The isolated MAGE-A12 HLA class I-binding peptide of claim 1 wherein the isolated peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, fragments thereof, and functional variants thereof.

3. The isolated MAGE-A12 HLA class I-binding peptide of claim 1 wherein the isolated peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, fragments thereof, and functional variants thereof.

4. An isolated MAGE-A12 HLA class I binding peptide comprising a fragment of the amino acid sequence of SEQ ID NO:2 which binds HLA Cw*07, or a functional variant thereof comprising one or more amino acid additions, substitutions or deletions, wherein the functional variant binds HLA Cw*07.

5. The isolated MAGE-A12 HLA class I-binding peptide of claim 1 or claim 4 wherein the isolated peptide is non-hydrolyzable.

6. The isolated MAGE-A12 HLA class I-binding peptide of claim 5 wherein the isolated peptide is selected from the group consisting of peptides comprising D-amino acids, peptides comprising a -psi[CH_2NH]-reduced amide peptide bond, peptides comprising a -psi[$COCH_2$]-ketomethylene peptide bond, peptides comprising a -psi[CH(CN)NH]-(cyanomethylene)amino peptide bond, peptides comprising a -psi[$CH_2CH(OH)$]-hydroxyethylene peptide bond, peptides comprising a -psi[CH_2O]-peptide bond, and peptides comprising a -psi[CH_2S]-thiomethylene peptide bond.

7. A composition comprising the isolated MAGE-A12 HLA class I-binding peptide of claim 1 and an isolated HLA class I- or class II-binding peptide of a non-MAGE-A12 tumor antigen.

8. A composition comprising the isolated MAGE-A12 HLA class I binding peptide of claim 4 and an isolated HLA class I- or class II-binding peptide of a non-MAGE-A12 tumor antigen.

9. The composition of claim 7 or claim 8, wherein the MAGE-A12 HLA class I-binding peptide and the HLA class I- or class II-binding peptide of a non-MAGE-A12 tumor antigen are combined as a polytope polypeptide.

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10. An isolated nucleic acid encoding a peptide selected from the group consisting of the peptide of any of claims 1-4, wherein the nucleic acid does not encode full length MAGE-A12.

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11. The isolated nucleic acid of claim 10, wherein the nucleic acid comprises a fragment of the nucleotide sequence of SEQ ID NO:1.

12. An expression vector comprising the isolated nucleic acid of claim 11 operably linked to a promoter.

13. The expression vector of claim 12 further comprising a nucleic acid which encodes an HLA-Cw*07 molecule.

14. A host cell transfected or transformed with an expression vector selected from the group consisting of the expression vector of claim 12 and the expression vector of claim 13.

15. A host cell transfected or transformed with the expression vector of claim 12, wherein the host cell expresses an HLA-Cw*07 molecule.

16. A method for enriching selectively a population of T lymphocytes with T lymphocytes specific for a MAGE-A12 HLA binding peptide comprising:

contacting a source of T lymphocytes which contains a population of T lymphocytes with an agent presenting a complex of the MAGE-A12 HLA binding peptide and an HLA

molecule in an amount sufficient to selectively enrich the population of T lymphocytes with the T lymphocytes specific for a MAGE-A12 HLA binding peptide.

17. The method of claim 16, wherein the agent is an antigen presenting cell contacted with a MAGE-A12 protein or an HLA binding fragment thereof.

18. The method of claim 16 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

19. A method for diagnosing a disorder characterized by expression of MAGE-A12 comprising:

contacting a biological sample isolated from a subject with an agent that is specific for a MAGE-A12 HLA binding peptide, and

determining the interaction between the agent and the MAGE-A12 HLA binding peptide as a determination of the disorder.

20. The method of claim 19 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

21. A method for diagnosing a disorder characterized by expression of a MAGE-A12 HLA binding peptide, comprising:

contacting a biological sample isolated from a subject with an agent that binds the complex; and

determining binding between the complex and the agent as a determination of the disorder.

22. The method of claim 21 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting (i) peptides which consist of a fragment of the amino acid sequence

of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

23. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of a MAGE-A12 HLA binding peptide sufficient to ameliorate the disorder.

24. The method of claim 23, wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

25. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of the composition of claim 7 or claim 8 sufficient to ameliorate the disorder.

26. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of an agent which enriches selectively in the subject the presence of complexes of an HLA molecule and a MAGE-A12 HLA binding peptide, sufficient to ameliorate the disorder.

27. The method of claim 26, wherein the agent comprises a MAGE-A12 HLA binding peptide.

28. The method of claim 26 or claim 27 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

29. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of autologous T lymphocytes sufficient to ameliorate the disorder, wherein the T lymphocytes are specific for complexes of an HLA molecule and a MAGE-A12 HLA binding peptide.

30. The method of claim 29 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

31. A method for identifying functional variants of a MAGE-A12 HLA binding peptide, comprising

selecting a MAGE-A12 HLA binding peptide, an HLA binding molecule which binds the MAGE-A12 HLA class I binding peptide, and a T cell which is stimulated by the MAGE-A12 HLA binding peptide presented by the HLA binding molecule;

mutating a first amino acid residue of the MAGE-A12 HLA binding peptide to prepare a variant peptide; and

determining the binding of the variant peptide to HLA binding molecule and the stimulation of the T cell, wherein binding of the variant peptide to the HLA binding molecule and stimulation of the T cell by the variant peptide presented by the HLA binding molecule indicates that the variant peptide is a functional variant.

32. The method of claim 31, wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, and (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6.

33. The method of claim 31, further comprising the step of comparing the stimulation of the T cell by the MAGE-A12 HLA binding peptide and the stimulation of the T cell by the functional variant as a determination of the effectiveness of the stimulation of the T cell by the functional variant.

Sub A3 34. An isolated polypeptide which binds selectively a polypeptide of any of claims 1-4, provided that the isolated polypeptide is not an HLA molecule.

35. The isolated polypeptide of claim 34, wherein the isolated polypeptide is an antibody.

36. The antibody of claim 35, wherein the antibody is a monoclonal antibody.

37. The isolated polypeptide of claim 34, wherein the isolated polypeptide is an antibody fragment selected from the group consisting of a Fab fragment, a $F(ab)_2$ fragment or a fragment including a CDR3 region selective for a MAGE-A12 HLA binding peptide.

38. An isolated T lymphocyte which selectively binds a complex of an HLA molecule and a MAGE-A12 HLA binding peptide.

39. The isolated T lymphocyte of claim 38 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

40. An isolated antigen presenting cell which comprises a complex of an HLA molecule and a MAGE-A12 HLA binding peptide.

41. The isolated antigen presenting cell of claim 40 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6 and (iii) functional variants of the peptides of (i) and (ii).

Sub A4 42. A vaccine composition comprising the polypeptide of any of claims 1-4 and a pharmaceutically acceptable carrier.

43. The vaccine composition of claim 42, further comprising an adjuvant.

Sub A5 44. A vaccine composition comprising a cell selected from the group consisting of a T lymphocyte of claims 38 and 39 and an antigen presenting cell of claims 40 and 41, and a pharmaceutically acceptable carrier.

45. The vaccine composition of claim 44, further comprising an adjuvant.

46. A vaccine comprising the isolated nucleic acid molecule of claim 10 and a pharmaceutically acceptable carrier.

47. The vaccine of claim 46, further comprising an adjuvant.

48. An isolated functional variant of a MAGE-A12 HLA binding peptide identified by the method of claim 31.

49. A method for identifying a candidate mimetic of a MAGE-A12 HLA binding peptide, comprising

providing a HLA molecule which binds the MAGE-A12 HLA binding peptide,

contacting the HLA molecule with a test molecule, and

determining the binding of the test molecule to the HLA molecule, wherein a test molecule which binds to the HLA molecule is a candidate mimetic of the MAGE-A12 HLA binding peptide.

50. The method of claim 49, further comprising

forming a complex of the HLA molecule and the candidate mimetic,

contacting the complex with a T cell which binds to a complex of an HLA molecule and the MAGE-A12 HLA binding peptide, and

assaying activation of the T cell.

51. The method of claim 50, wherein activation of the T cell is indicated by a property selected from the group consisting of proliferation of the T cell, interferon-γ production by the

T cell, tumor necrosis factor production by the T cell, and cytolysis of a target cell by the T cell.

52. A protein microarray comprising an isolated MAGE-A12 HLA class I-binding peptide or a functional variant thereof which binds HLA class I molecules comprising one or more amino acid additions, substitutions or deletions.

53. The protein microarray of claim 52, wherein the isolated MAGE-A12 HLA class I-binding peptide comprises the amino acid sequence of SEQ ID NO:6.

54. The protein microarray of claim 52, wherein isolated MAGE-A12 HLA class I-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, and functional variants thereof.

55. A method for diagnosing a disorder characterized by expression of MAGE-A12 comprising,

contacting the protein microarray of claim 52 with a biological sample isolated from a subject suspected of having the disorder, and

determining the binding of a constituent of the biological sample to the isolated MAGE-A12 HLA class I binding peptide.

56. The method of claim 55, wherein the constituent of the biological sample is selected from the group consisting of an antibody, a T lymphocyte, and a HLA molecule.

57. The method of claim 55, wherein the disorder is cancer.

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